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ISCHAEMIC HEART DISEASE

Bivalirudin as an alternative to heparin and abciximab in PCI? ► Bivalirudin is a direct thrombin inhibitor that is being investigated as a potential replacement for heparin. The results of the REPLACE-2 (randomized evaluation in PCI linking Angiomax to reduced clinical events) trial last year demonstrated that at 30 days following percutaneous coronary intervention (PCI), intraprocedural administration of bivalirudin with a glycoprotein (Gp) IIb/IIIa antagonist provided similar protection from acute ischaemic events with fewer haemorrhagic complications than the combination of heparin and Gp IIb/IIIa inhibition. Follow up data reveal comparable rates of death (1.4% of patients in the heparin group *v* 1.0% of patients in the bivalirudin group; p = 0.15), myocardial infarction (7.4% *v* 8.2%; p = 0.24) and repeat revascularisation (11.4% *v* 12.1%; p = 0.45) at six months. An ongoing large scale trial (acute catheterization and urgent intervention triage strategy (ACUITY)) is now testing the efficacy of bivalirudin with or without Gp IIb/IIIa blockade in high risk patients.

▲ **Lincoff AM**, Kleiman NS, Kereiakes DJ, *et al*. Long-term efficacy of bivalirudin and provisional glycoprotein IIb/IIIa blockade vs heparin and planned glycoprotein IIb/IIIa blockade during percutaneous coronary revascularization. *JAMA* 2004;**292**:696–703.

Magnesium prophylaxis reduces cardiac arrhythmias post-CABG, but not length of stay ► Previous data highlight the problems of post-coronary artery bypass graft (CABG) atrial fibrillation and other arrhythmias. Length of stay increases, and mortality may be affected. This study, a meta-analysis of 17 trials (n = 2069 patients) showed serum magnesium concentration at 24 hours after surgery in the treatment group was significantly higher than that in the control group (weighted mean difference 0.45 mmol/l, 95% confidence interval (CI) 0.30 to 0.59 mmol/l; p < 0.001). Magnesium supplementation reduced the risk of supraventricular arrhythmias (relative risk (RR) 0.77, 95% CI 0.63 to 0.93; p = 0.002) and ventricular arrhythmias (RR 0.52, 95% CI 0.31 to 0.87; p < 0.0001), but had no effect on the length of hospital stay (weighted mean difference −0.28 days, 95% CI −0.70 to 1.27 days; p = 0.48), the incidence of perioperative myocardial infarction (RR 1.03, 95% CI 0.52 to 2.05; p = 0.99), or mortality (RR 0.97, 95% CI 0.43 to 2.20; p = 0.94). Why length of stay was not affected is not clear.

▲ **Shiga T**, Wajima Z, Inoue T, Ogawa R. Magnesium prophylaxis for arrhythmias after cardiac surgery: a meta-analysis of randomized controlled trials. *Am J Med* 2004;**117**:325–33.

Choosing an old hand or a young buck as your cardiac surgeon ► A total of 18 913 patients underwent coronary artery surgery for the first time between April 1997 and March 2003 in the north of England, 5678 of whom were operated on by 15 surgeons in the first four years after their consultant appointment. Observed and predicted mortality (EuroSCORE) for surgeons in their first, second, third, and fourth years after appointment as a consultant were compared with figures for established surgeons. Overall mortality decreased over the six years of study (p = 0.01). Of the patients operated on by established surgeons or newly appointed consultants, 265/13 235 (2.0%) and 109/5678 (1.9%), respectively, died (p = 0.71). There was a progressive decrease in observed mortality with time after appointment as a consultant from 2.2% in the first year to 1.2% in the fourth year (p = 0.049). This result remained significant after adjustment for time and case mix (p = 0.019). The reasons for the improvement over four years are not clear. Artefact or bias may be involved rather than a real effect.

▲ **Bridgewater B**, Grayson AD, Au J, Hassan R, Dihmis WC, Munsch C, Waterworth P. Improving mortality of coronary surgery over first four years of independent practice: retrospective examination of prospectively collected data from 15 surgeons. *BMJ* 2004;**329**:421.

New evidence about the old coronary risk factors ► Although more than 80% of the global burden of cardiovascular disease occurs in low income and middle income countries, knowledge of the importance of risk factors is largely derived from developed countries. A standardised case–control study of acute myocardial infarction in 52 countries, representing every inhabited continent, was performed, with 15 152 cases and 14 820 controls enrolled. Odds ratios and their 99% CIs for the association of risk factors to myocardial infarction and their population attributable risks (PAR) were calculated. Smoking (odds ratio (OR) 2.87 for current *v* never, PAR 35.7% for current and former *v* never), raised ApoB/ApoA1 ratio (OR 3.25 for top *v* lowest quintile, PAR 49.2% for top four quintiles *v* lowest quintile), history of hypertension (OR 1.91, PAR 17.9%), diabetes (OR 2.37, PAR 9.9%), abdominal obesity (OR 1.12 for top *v* lowest tertile and 1.62 for middle *v* lowest tertile, PAR 20.1% for top two tertiles *v* lowest tertile), psychosocial factors (OR 2.67, PAR 32.5%), daily consumption of fruits and vegetables (OR 0.70, PAR 13.7% for lack of daily consumption), regular alcohol consumption (OR 0.91, PAR 6.7%), and regular physical activity (OR 0.86, PAR 12.2%) were all significantly related to acute myocardial infarction (p < 0.0001 for all risk factors and p = 0.03 for alcohol). These associations were noted in men and women, old and young, and in all regions of the world. Collectively, these nine risk factors accounted for 90% of the PAR in men and 94% in women.

▲ **Yusuf S**, Hawken S, Ôunpuu S, Dans T, Avezum A, Lanas F, McQueen M, Budaj A, Pais P, Varigos J, Lisheng L, on behalf of the INTERHEART Study Investigators. Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study): case-control study. *Lancet* 2004;**364**;on line.

Nifedipine GITS is still a good antianginal agent ► Some years ago a scare was raised about the use of calcium channel blockers, in particular nifedipine, in patients with coronary disease. A total of 3825 patients with treated stable symptomatic coronary disease were assigned to double blind addition of nifedipine GITS (gastrointestinal therapeutic system) 60 mg once daily and 3840 to placebo. The primary end point was the combination of death, acute myocardial infarction, refractory angina, new overt heart failure, debilitating stroke, and peripheral revascularisation. Mean (SD) follow up was 4.9 (1.1) years. Analysis was by intention to treat. In all, 310 patients allocated nifedipine died (1.64 per 100 patient-years) compared with 291 people allocated placebo (1.53 per 100 patient-years; hazard ratio (HR) 1.07, 95% CI 0.91 to 1.25; p = 0.41). Primary end point rates were 4.60 per 100 patient-years for nifedipine and 4.75 per 100 patient-years for placebo (HR 0.97, 95% CI 0.88 to 1.07; p = 0.54). With nifedipine, rate of death and any cardiovascular event or procedure was 9.32 per 100 patient-years versus 10.50 per 100 patient-years for placebo (HR 0.89, 95% CI 0.83 to 0.95; p = 0.0012). The difference was mainly attributable to a reduction in the need for coronary angiography and interventions in patients assigned nifedipine, despite an increase in peripheral revascularisation. Nifedipine had no effect on the rate of myocardial infarction.

▲ **Poole-Wilson PA**, Lubsen J, Kirwan B-A, *et al* on behalf of the ACTION (A Coronary disease Trial Investigating Outcome with Nifedipine gastrointestinal therapeutic system) Investigators. Effect of long-acting nifedipine on mortality and cardiovascular morbidity in patients with stable angina requiring treatment (ACTION trial): randomised controlled trial. *Lancet* 2004;**364**:849–57.

A statin should be on the CARDS for all diabetics ► Type 2 diabetes is associated with a substantially increased risk of cardiovascular disease. Most cardiologists treat cholesterol aggressively in this group of patients anyway. Now the trial data prove them right. A total of 2838 patients aged 40–75 years in 132 centres in the UK and Ireland were randomised to placebo (n = 1410) or atorvastatin 10 mg daily (n = 1428). Study

entrants had no documented previous history of cardiovascular disease, an LDL cholesterol < 4.14 mmol/l, a fasting triglyceride < 6.78 mmol/l, and at least one of the following: retinopathy, albuminuria, current smoking, or hypertension. The primary end point was time to first occurrence of the following: acute coronary heart disease events, coronary revascularisation, or stroke. The trial was terminated two years earlier than expected because the pre-specified early stopping rule for efficacy had been met. Median duration of follow up was 3.9 years (interquartile range (IQR) 3.0–4.7). One hundred and twenty seven patients allocated placebo (2.46 per 100 person-years at risk) and 83 allocated atorvastatin (1.54 per 100 person-years at risk) had at least one major cardiovascular event (rate reduction 37%, 95% CI −52 to −17; p = 0.001). Treatment would be expected to prevent at least 37 major vascular events per 1000 such people treated for four years. Assessed separately, acute coronary heart disease events were reduced by 36% (95% CI −55% to −9%), coronary revascularisations by 31% (95% CI −59% to 16%), and rate of stroke by 48% (95% CI −69% to −11%). Atorvastatin reduced the death rate by 27% (95% CI −48% to 1%, p = 0.059). The debate about whether all people with this disorder warrant statin treatment should now focus on whether any patients are at sufficiently low risk for this treatment to be withheld.

▲ **Colhoun HM**, Betteridge DJ, Durrington PN, Hitman GA, Neil HAW, Livingstone SJ, Thomason MJ, Mackness MI, Charlton-Menys V, Fuller JH, on behalf of the CARDS Investigators. Primary prevention of cardiovascular disease with atorvastatin in type 2 diabetes in the collaborative atorvastatin diabetes study (CARDS): multicentre randomised placebo-controlled trial. *Lancet* 2004;**364**:685–96.

Drug eluting stents reduce restenosis but not mortality (yet?) ► A systematic literature search aimed to identify all randomised clinical trials with 6–12 months of clinical follow up of bare metal stents (BMS) versus drug eluting stents (DES). The primary outcomes examined were rates of death, myocardial infarction, target lesion revascularisation, major adverse cardiac events (death, myocardial infarction, and target vessel revascularisation), and angiographic restenosis. The authors identified 11 eligible trials involving 5103 patients. The pooled mortality rates were low for both DES and BMS with no evidence of any difference between them (OR 1.11, 95% CI 0.61 to 2.06). Pooled rates of myocardial infarction showed no between-group difference (OR 0.92, 95% CI 0.65 to 1.25). The rate of major adverse cardiac events was 7.8% with DES and 16.4% with BMS (OR 0.42, 95% CI 0.32 to 0.53), and the angiographic restenosis rates were also lower for DES (8.9% *v* 29.3%; OR 0.18, 95% CI 0.06 to 0.40). The pooled rates of major adverse cardiac events for each DES type and the respective BMS were: for sirolimus, 6.8% *v* 21.0% (OR 0.28, 95% CI 0.17 to 0.41); for polymer based paclitaxel 8.7% *v* 16.7% (OR 0.47, 95% CI 0.25 to 0.71); and for non-polymer based paclitaxel 7.7% *v* 9.5% (OR 0.64, 95% CI 0.42 to 1.00). There were no significant changes in rates of edge restenosis, stent thrombosis, or late incomplete stent apposition with DES, although the confidence intervals were wide.

▲ **Babapulle MN**, Joseph L, Bélisle P, Brophy JM, Eisenberg MJ. A hierarchical Bayesian meta-analysis of randomised clinical trials of drug-eluting stents. *Lancet* 2004;**364**:583–91.

Defibrillators and not paramedics with ACLS skills are the way to reduce death from cardiac arrest ► Rate of survival after out-of-hospital cardiac arrest is low. A trial of randomly assigned community units (for example, shopping malls and apartment complexes) to a structured and monitored emergency response system involving lay volunteers trained in cardiopulmonary resuscitation (CPR) alone or in CPR and the use of automated defibrillators (AEDs) recruited more than 19 000 volunteer responders from 993 community units in 24 North American regions. Patients with treated out-of-hospital cardiac arrest in the two groups were similar in age (mean 69.8 years), proportion of men (67%), rate of cardiac arrest in a public location (70%), and rate of witnessed cardiac arrest (72%). No inappropriate shocks were delivered. There were more survivors to hospital discharge in the units assigned to have volunteers trained in CPR plus the use of AEDs (30 survivors among 128 arrests) than there were in the units assigned to have volunteers trained only in CPR (15 among 107; RR 2.0, 95% CI 1.07 to 3.77; p = 0.03). On the other hand, in a separate study, adding advanced life support training (ACLS) for paramedics increased significantly the rate of admission to a hospital (10.9% *v* 14.6%, p < 0.001), but the rate of survival to hospital discharge did not change (5.0% *v* 5.1%, p = 0.83).

▲ **The Public Access Defibrillation Trial Investigators**. Public-access defibrillation and survival after out-of-hospital cardiac arrest. *N Engl J Med* 2004;**351**:637–46.

▲ **Stiell IG**, Wells GA, Field B, *et al*, for the Ontario Prehospital Advanced Life Support Study Group. Advanced cardiac life support in out-of-hospital cardiac arrest. *N Engl J Med* 2004;**351**:647–56.

GENERAL CARDIOLOGY

Little evidence for echocardiography in haemodynamically stable pulmonary embolism ► Echocardiographically assessed right ventricular dysfunction is increasingly used to guide more aggressive treatment in haemodynamically stable patients with acute pulmonary embolism (PE). Seven studies were included in a meta-analysis. All had methodologic shortcomings, but they suggested an at least twofold increased risk of PE related mortality in patients with right ventricular dysfunction, the prevalence of which varied from 40–70%. However, this seems to be less convincing in haemodynamically stable patients. The only two studies that allowed for an estimation of the accuracy in normotensive patients showed low positive predictive values of echocardiographic right ventricular dysfunction for PE related in-hospital mortality (positive predictive value, 4% and 5% in the two studies).

▲ **ten Wolde M**, Söhne M, Quak E, Mac Gillavry MR, Büller HR. Prognostic value of echocardiographically assessed right ventricular dysfunction in patients with pulmonary embolism. *Arch Intern Med* 2004;**164**:1685–9.

Endovascular aneurysm repair is a viable alternative to open operation ► Endovascular aneurysm repair (EVAR) is a new technology to treat patients with abdominal aortic aneurysm (AAA) when the anatomy is suitable. Uncertainty exists about how endovascular repair compares with conventional open surgery. EVAR trial 1 was instigated to compare these treatments in patients judged fit for open AAA repair. Between 1999 and 2003, 1082 elective (non-emergency) patients were randomised to receive either EVAR (n = 543) or open AAA repair (n = 539). Patients aged > 60 years with aneurysms of diameter > 5.5 cm, who were fit enough for open surgical repair (anaesthetically and medically well enough for the procedure), were recruited for the study at 41 British hospitals proficient in the EVAR technique. Patients (983 men, 99 women) had a mean age of 74 years and mean AAA diameter of 6.5 cm; 1047 (97%) patients underwent AAA repair and 1008 (93%) received their allocated treatment. Thirty day mortality in the EVAR group was 1.7% (9/531) versus 4.7% (24/516) in the open repair group (OR 0.35, 95% CI 0.16 to 0.77; p = 0.009). By per-protocol analysis, 30 day mortality for EVAR was 1.6% (8/512) versus 4.6% (23/496) for open repair (OR 0.33, 95% CI 0.15 to 0.74; p = 0.007). Secondary interventions were more common in patients allocated EVAR (9.8% *v* 5.8%, p = 0.02). Any change in clinical practice should await durability and longer term results, however. In addition, all patients should have a thorough cardiovascular workup to try to reduce cardiac risk perioperatively. The EVAR 2 study will report on medical treatment versus EVAR in patients thought medically unfit for open surgery.

▲ **The EVAR Trial Participants**. Comparison of endovascular aneurysm repair with open repair in patients with abdominal aortic aneurysm (EVAR trial 1), 30-day operative mortality results: randomised controlled trial. *Lancet* 2004;**364**:843–48.

Journals scanned

American Journal of Medicine; American Journal of Physiology: Heart and Circulatory Physiology; Annals of Emergency Medicine; Annals of Thoracic Surgery; Archives of Internal Medicine; BMJ; Chest; European Journal of Cardiothoracic Surgery; Lancet; JAMA; Journal of Clinical Investigation; Journal of Diabetes and its Complications; Journal of Immunology; Journal of Thoracic and Cardiovascular Surgery; Nature Medicine; New England Journal of Medicine; Pharmacoeconomics; Thorax

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